

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SCB 471 PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/00618	International filing date (day/month/year) 01/02/1999	Priority date (day/month/year) 03/02/1998
International Patent Classification (IPC) or national classification and IPC G01N33/569		
Applicant BRACCO S.P.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  05/08/1999	Date of completion of this report  29.03.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Herrero, M  Telephone No. +49 89 2399 8542 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/00618

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-21 as published

**Claims, No.:**

1-14 as published

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	2, 5, 6, 8, 10, 11, 14
	No:	Claims	1, 3, 4, 7, 9, 12, 13
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

**INTERNATIONAL PRELIMINARY  
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**2. Citations and explanations**

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

## SECTION V

### 2. CITATIONS AND EXPLANATIONS

2.1 The following documents have been considered for the purposes of this report:

D1: Karamanos, N.K. et al (1997) Arch. Biochem. Biophys. **342**:389-395  
D2: GB-A-992132

### 2.2 Novelty and inventive step (Art. 33(2) and (3) PCT)

The present application does not satisfy the criteria set forth in Article 33(2) and (3) PCT because,

- a) the subject-matter of Claims 1, 3, 4, 7, 9, 12 and 13 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT)
- b) the subject-matter claimed does not involve an inventive step (Rule 65(1)(2) PCT).

The technical problem underlying the present application relates to the provision of a simplified procedure useful for the direct determination/diagnosis of prosthetic infections caused by pathogenic slime-producing strains of staphylococci.

The underlying problem was known in the art and solutions thereto had been proposed, e.g. in D1 (see e.g. page 394, right column, lines 22-31), which are equivalent to the solution hereby claimed.

Document D1 discloses a method suitable for the diagnosis of *Staphylococcus epidermidis* infection by direct analysis in blood sera which differentiates among slime-positive and slime-negative strains and which distinguishes slime-producing *S. epidermidis* from other staphylococci species by simple laboratory tests. The performance of the method relies on the use of a sulfated 20-kDa acidic

polysaccharide antigen (the 20-kDa PS) which is the major component (60-65%) of the total extracellular slime carbohydrate produced by *S. epidermidis* slime-producing strains.

In view of the relevant disclosures of D1, the subject-matter of Claims 1, 3, 4, 7, 9, 12 and 13 lacks novelty and/or inventiveness (Art. 33(2) and (3) PCT).

In the context of the present application the preferred embodiment of dependent Claim 2, i.e. the detection according to the method of Claim 1 of IgG and IgM antibodies, is obvious (Art. 33(3) PCT).

Likewise the preferred embodiments of dependent Claim 7, i.e. possible assay formats for the detection method of Claim 1, merely represent the application of optional techniques well known to the skilled person (Art. 33(3) PCT).

The process for preparing a polysaccharide from *Staphylococcus* cultures according to Claim 8, is regarded as novel over the available prior art. However, the application as originally filed does not provide evidence of a technical nature suitable to ascertain whether the performance of the claimed process is associated with any advantageous/unexpected effect over related processes of the state of the art [e.g. over the corresponding procedure mentioned on page 390 (right column) of D1 or the method employed in Example 1 of D2 to prepare polysaccharide from a stock culture of a *Staphylococcus aureus* strain], which evidence could substantiate the presence of an inventive step and therefore the claimed process does not satisfy the requirements of Art. 33(3) PCT.

When discussing the results of the assays carried out employing the 20-kDa PS purified from *S. epidermidis*, D1 concludes that "this component is a principal antigenic determinant of the extracellular slime layer and, consequently, it can be thought of as the main representative of the whole mixture" (see D1, page 394 right column, lines 19-22).

In connection with the above it has to be emphasized that, taking into consideration the polysaccharide of D1, the product obtainable by the process of Claim 8 seems to be neither novel nor inventive (Art. 33(2) and (3) PCT). These

objections would be reinforced should the starting cultures employed in the process of Claim 8 belong to the slime-producing *S. epidermidis* strain identified in the application by the arbitrary denomination SA1545.

Moreover, in view of the passage on page 4, lines 20-22 of the present description which states that: "Experiments were also indicative when performed using the *Staphylococcus aureus* strain deposited by the applicant at DSMZ No. 11942" it had to be considered that in order to solve the underlying technical problem, the use of said deposited strain as the source of the polysaccharide of interest does not result in any advantageous/unexpected effect over the use of e.g. the polysaccharide obtained from the (non-deposited) specific *S. epidermidis* strain identified in the application by the arbitrary denomination SA1545.

In line with the above, the provision of the deposited strain *Staphylococcus aureus* DSMZ No. 11942 does not appear to result in any special effect whatsoever which could substantiate this strain as inventive and consequently Claim 14 directed to this deposited strain *per se* would not appear to satisfy the criterion set forth in Art. 33(3) PCT.

Under these circumstances, neither the method of Claim 5, which relies on the use of the polysaccharide produced by the deposited strain DSMZ No. 11942, nor the method of Claim 6, which relies on the use of the polysaccharide obtainable from any of the staphylococcal sources mentioned in Claims 1-5 according to the process of Claim 8, can be regarded as involving an inventive step, contrary to the requirements of Art. 33(3) PCT. A similar objection (Art. 33(3) PCT) applies *mutatis mutandis* to Claim 13 directed to an expected use of the polysaccharide of Claim 9.

Furthermore, insofar as the relevant constituting components of the kits according to Claims 10 and 11 would also appear to lack novelty and/or inventive step, Claims 10 and 11 cannot be regarded as inventive. It should be kept in mind that, irrespective of their intended use, any claimed kit of parts has to meet *per se* the novelty and inventive step requirements of Art. 33(2) and (3) PCT.

**SECTION VII**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.

**SECTION VIII**

1. The following expressions appear to contain clerical mistakes:

"surnatant" : page 5, lines 4, 5 and 11 and Claim 24, steps (c), (d) and (g)

"periprotetic" : page 6, line 12

2. Claim 11 should have referred back to Claim 10.

E.K

PCT/EP99/00618

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

18 October 1999 (18.10.99)

International application No.

PCT/EP99/00618

Applicant's or agent's file reference

SCB 471 PCT

International filing date (day/month/year)

01 February 1999 (01.02.99)

Priority date (day/month/year)

03 February 1998 (03.02.98)

Applicant

THALLER, Maria, Cristina et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

05 August 1999 (05.08.99)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
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# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>SCB 471 PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 99/ 00618</b>	International filing date (day/month/year) <b>01/02/1999</b>	(Earliest) Priority Date (day/month/year) <b>03/02/1998</b>
Applicant  <b>BRACCO S.P.A. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

T/EP 99/00618

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 G01N33/569 C12N1/20 C12P19/04

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 G01N C12N C12P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KARAMANOS, N. K. ET AL: "The major 20 kDa polysaccharide of Staphylococcus epidermidis extracellular slime and its antibodies as powerful agents for detecting antibodies in blood serum and differentiating among slime-positive and -negative S. epidermidis and other staphylococci species" ARCH. BIOCHEM. BIOPHYS. (1997), 342(2), 389-395 CODEN: ABBIA4; ISSN: 0003-9861, XP002104457 see the whole document --- -/--	1-12



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

1 June 1999

Date of mailing of the international search report

23/06/1999

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Authorized officer

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